40 mL of CH_2Cl_2. The solvent was evaporated, the residue redissolved in CH_2Cl_2, and the solvent was evaporated. The crude **15** weighed 740 mg (98%) and was recrystallized from MeCN. The infrared spectra of **15** prepared from **5** with EtO_2CCHN_2 and with Me_2SCHCO_2Et were identical.

Synthesis of 13a. To a stirred suspension of 211 mg (0.59 mmol) of **8** in 6.43 g of CH_2Cl_2 was added 253 mg (2.22 mmol) of N_2CHCO_2Et. After 17 h the solvent was evaporated, the residue was dissolved in 4 mL of CH_2Cl_2, and the solvent was evaporated. The crude **13a** weighed 232 mg (89%) and melted at 145–141 °C. Recrystallization from MeCN gave **13a**: mp 148–131 °C.

Hydrolysis of 13. A suspension of 123 mg (0.30 mmol) of **13**, 393 mg MeCN, and 369 mg of H_2O was stirred for 29 h during which time the color of the mixture changed from creamy white to yellow. Filtration gave 77 mg (79%) of **14**.[3] The filtrate was subjected to GC–mass spectroscopy. The presence of EtO_2CCHO was verified by its molecular ion m/e 102 and by a comparison with an authentic sample with its fragmentation pattern and retention time.

Synthesis of 15. A mixture of 95 mg (0.23 mmol) of **5** in 2 mL of MeOH was refluxed for 45 min. The solution was cooled and filtered. The crude **15** weighed 94 mg (92%). Recrystallization from MeOH gave **15**: mp 109–112 °C; IR (Nujol) 3330, 1730, 1725, 1620, 1325, 1365, 1260, 1135, 1095, 1060, 1040, 1010, 870, 862, 848, 713 cm^{-1}; ^1H NMR (90 MHz) ($CDCl_3$) δ 1.25 (t, 3 H), 3.11 (s, 3 H), 4.22 (q, 4 H), 5.24 (d, 1, CH), 5.45 (d, 1, NH), 7.09 (d, 1 H), 7.32 (d, 1 H), 8.37 (s, 4 H).

Synthesis of 17. Compound **17** was prepared by the dropwise addition of a solution of 45.7 mg (0.39 mmol) of $PhCHN_2$ in 0.3 mL of CH_2Cl_2 to a solution of 122 mg (0.38 mmol) of **5** in 2.5 mL of CH_2Cl_2. Nitrogen evolution was instantaneous and the orange color of **5** was discharged. The solvent was evaporated and the 131 mg (96%) of **17** was recrystallized from MeCN to give **17**: mp 198–201 °C.

Synthesis of 18. To a solution of 145 mg (0.45 mmol) of **5** in 2 mL of CH_2Cl_2 was added dropwise a solution of 88 mg (0.45 mmol) of diphenyldiazomethane in 0.2 mL of CH_2Cl_2. Nitrogen evolution was complete in a few minutes. After about 4 h pentane was added and then the solvent was evaporated. The residue was slurried in pentane and the crude **18** (140 mg, 28.5%) was filtered off. Recrystallization from MeCN gave **18**: mp 204–208 °C.

Synthesis of 19. A solution of 276 mg (1.06 mmol) of **3** in 25 mL of CH_2Cl_2 was added dropwise and with stirring to a solution containing a slight excess of phenyldiazomethane in 100 mL of CH_2Cl_2. After 3 h the solvent was evaporated to about 13 mL. The solution was filtered and the crude **19** (230 mg, 65.4%) recrystallized from methanol to give **21** melting at 114–117 °C.

Synthesis of 25. A mixture of 164 mg (0.50 mmol) of **5** and 131 mg (0.50 mmol) of $(C_6H_5)_3P$ in 2 mL of CH_2Cl_2 stood 17 h at ambient temperature. The solvent was evaporated and the residue slurried with methanol. Filtration gave 111 mg (0.36 mol, 72%) of crude **25**, mp 168–176 °C. Recrystallization from 2-propanol gave **25** melting at 183–187 °C.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by The American Chemical Society, and to the National Science Foundation for Grant CHE-84058555. We thank Professor Xavier Creary for running the reaction of **5** with diphenyldiazomethane and Mr. Jim Spriggle for mass spectral data.

Registry No. **5**, 90388-37-7; **7a**, 100189-94-4; **7b**, 100189-95-5; **7c**, 100189-96-6; **7d**, 100189-97-7; **7e**, 100189-98-8; **8**, 100205-35-4; **9**, 100189-99-9; **10**, 100190-00-9; **11**, 67944-81-4; **12**, 100190-01-0; **13**, 100190-02-1; **13a**, 100190-03-2; **14**, 90368-43-7; **15**, 100190-04-3; **16**, 7380-81-6; **17**, 100190-05-4; **18**, 100190-06-5; **19**, 100190-07-6; **25**, 100190-08-7; $PhCHN_2$, 21113-61-1; Me_2SO, 67-68-5; methyl phenyl sulfoxide, 1193-82-4; benzyl methyl sulfoxide, 824-86-2; tetramethylene sulfoxide, 1600-44-8; dibenzyl sulfoxide, 621-08-9; ethyl diazoacetate, 623-73-4; diphenyldiazoethane, 883-40-9; triphenylphosphine, 603-35-0.

Supplementary Material Available: Crystal structure data for **7a** and ^{13}C NMR spectral data for **7a** and **12**, IR spectral data for **7a–e**, **10**, and **12** (8 pages). Ordering information is given on any current masthead page.

Kinetics of Reversible Endothermic Elimination Reactions: β-Amino Carboxylic Esters and Amides

Mark R. Johnson

Functional Polymers and Process Research Laboratory, The Dow Chemical Company, Midland, Michigan 48674

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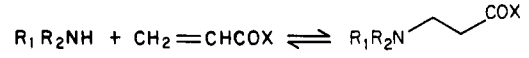
The kinetics of the elimination reactions of substituted β-amino carboxylic esters and amides, to give amines and the α,β-unsaturated esters and amides, have been studied in several model systems. The reaction was studied by trapping the olefin formed with another nucleophile capable of competing with the amine formed by elimination. The rate constant for elimination of methyl 3-(*N*-methyl-*N*-butylamino)propionate, in methanol at room temperature, is 1.8×10^{-6} s^{-1}. The corresponding amide has an elimination rate constant of 8.8×10^{-8} s^{-1}. Rate constants for the forward reaction were also measured and combined with the reversion rate constants to yield equilibrium constants for the same two systems. The equilibrium constant for the methyl esters is 2.0×10^4 L mol^{-1} and for the amides is 7.3×10^3 L mol^{-1}. These were confirmed by measurement of the equilibrium concentrations of olefins by ^1H NMR spectroscopy.

The addition reaction of amines with α,β-unsaturated ketones, esters, amides, and sulfones is a well-known reaction whose kinetics have been studied in some detail.[1] It has been recognized that this reaction is reversible, and this reversion reaction has been used in the synthesis of substituted acrylamides[2] and certain β-amino ketones.[3]



Similar reversion reactions with oxygen and sulfur nucleophiles have been studied,[4] and in some cases the kinetics as well as the equilibrium concentrations of the

(1) (a) Shenhav, H.; Rappoport, Z.; Patai, S. *J. Chem. Soc. B* **1970**, 469. (b) McDowell, S. T.; Stirling, C. J. *J. Chem. Soc. B* **1970**, 343. (c) Ogata, N.; Asahara, T. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 1486. (d) Sanui, K.; Ogata, N. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 1968.

(2) (a) Erickson, J. G. *J. Am. Chem. Soc.* **1952**, *74*, 6281. (b) Moss, P. H. U.S. Patent 3 878 247, 1975. (c) Barron, B. G. U.S. Patent 3 652 671, 1972.

(3) (a) Craig, J. Cymerman; Johns, S. R.; Moyle, M. *J. Org. Chem.* **1963**, *28*, 2779. (b) Craig, J. Cymerman; Moyle, M.; Johnson, L. F. *J. Org. Chem.* **1964**, *29*, 410. (c) Cromwell, N. H.; Soriano, D. S.; Doomes, E. *J. Org. Chem.* **1980**, *45*, 4983.

(4) (a) Mayer, B. J.; Spencer, T. A.; Onan, K. D. *J. Am. Chem. Soc.* **1984**, *106*, 6343. (b) Mayer, B. J.; Spencer, T. A. *J. Am. Chem. Soc.* **1984**, *106*, 6349. (c) Barladi, P. G. et al. *J. Chem. Soc., Chem. Commun.* **1982**, 1265. (d) Kupchan, S. M.; Giacobbe, T. J.; Krull, I. S. *Tetrahedron Lett.* **1970**, 2859.

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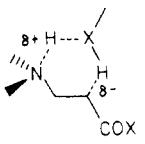
reaction components have been determined. In the case of the amines, however, little quantitative work has been reported. Given the relevance of this reaction to the synthesis of substituted acrylamides and the stability of amine-activated olefin adducts,[5] we have examined the kinetics of the elimination in several model systems.

Results and Discussion

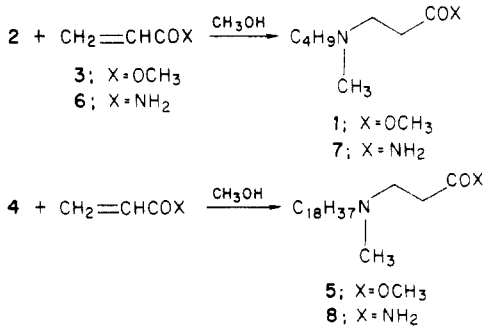
Description of Model System. The addition reactions of amines with alkyl acrylates and acrylamides essentially "go to completion" in most cases. In order to study the rate of the reverse reaction we need to devise a system in which one of the species, either the amine or the olefin, is removed from the equilibrium by a suitable trap. To make such a system amenable to a simple kinetic analysis, we should like the rate of the trapping reaction to be either very fast when compared to the forward reaction or nearly the same. A system which fits the latter description is shown in Scheme I. The adduct 1 derived from the addition of methylbutylamine (2) to methyl acrylate (3) is allowed to equilibrate with octadecylmethylamine (4), giving the adduct 5, from octadecylmethylamine and methyl acrylate, along with methylbutylamine. Of course, the equilibrium could be approached from either side. In this case, the rates of addition and reversion of the two amines with methyl acrylate turn out to be virtually identical, leading to a simple kinetic analysis (see below). Substitution of acrylamide for methyl acrylate in Scheme I gives the analogous amide system, which we have also examined.

The literature on the kinetics of the addition reactions of amines and activated olefins allows us to select reaction conditions giving accessible rates and straightforward rate expressions. In aprotic solvents, the reaction is third order, second order in amine and first order in olefin.[1a,b] This is attributed to a requirement for a third species to participate in proton transfer at the transition state. In protic



solvents like methanol, the solvent serves this function, and the reaction is pseudo second order and also much faster.

Synthesis and Equilibration Experiments. Reaction of methylbutylamine or octadecylmethylamine with methyl acrylate at room temperature in methanol gave the desired addition products in quantitative yield. Reaction of the



same amines with acrylamide gave the corresponding amide addition products.

(5) Barbucci, R. et al. *Macromolecules* **1983**, *16*, 456. (b) Robinson, J. B.; Thomas, J. *J. Chem. Soc.* **1965**, 2271. (c) Ganellin, C. R.; Spickett, R. G. W. *J. Med. Chem.* **1965**, *8*, 619. (d) Carabateas, P.; Grunbach, L. *J. Med. Chem.* **1962**, *5*, 913.

Scheme I

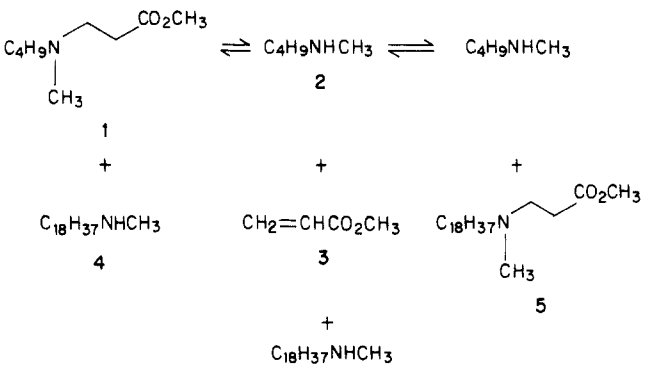


Table I. Reaction of 1 with Octadecylmethylamine in Methanol[a]

temp, °C	time, h	ratio 1/5
23	1.2	98.5/1.5 (±0.5)
23	3.5	97.3/2.7
23	5.5	95.4/4.6
23	24	87.4/12.6
23	48	77.9/22.1
23	72	69.2/30.8
23	96	64.9/35.1
120	1.0	49.6/50.4
120	4.5	49.7/50.3

[a] $[1]_0 = [4]_0 = 0.289$ M.

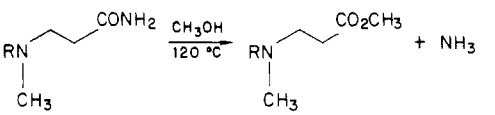
Table II. Reaction of 1 with Octadecylmethylamine in Acetonitrile at 120 °C[a]

time, h	ratio 1/5
1.0	97.5/2.5 (±0.5)
4.0	91.4/8.6
21	56.8/43.2

[a] $[1]_0 = [4]_0 = 0.289$ M.

Preliminary equilibration experiments were done in methanol at room temperature and at 120 °C (Parr reactor). Treatment of a solution of amino ester 1 with an equimolar amount of amine 4 (0.289 M) at 120 °C gave a 1/1 mixture of adducts 1 and 5 in less than 1 h (SEC analysis). The only other species present in significant amounts were amines 2 and 4. This composition was unchanged after an additional 3.5 h at 120 °C. At room temperature, the same reaction mixture gives the same product composition in several weeks, but formation of 5 is easily detected after several hours. This data is summarized in Table I. When the same equilibration reaction is done in acetonitrile at 120 °C, reaction is much slower, with only a small amount of 5 present after 1 h. After 21 h, equilibration is still incomplete (Table II). The same reaction could not be done at room temperature due to the limited solubility of 4 in acetonitrile. These results are consistent with the known solvent effects on the rates of the forward reactions.[1]

The corresponding reactions of the acrylamide derivatives were also examined. When a methanol solution containing equimolar amounts of 4 and 7 (0.289 M) was heated at 120 °C for 1 h, an approximately 2/1 ratio of 7/8 was observed (Table III). When the solution was heated for 20 h at 120 °C, a mixture of amides 7 and 8, along with methyl esters 1 and 5, was obtained. The esters, no doubt,



arise from reaction of solvent with the amides. On further

Table III. Reaction of 7 with Octadecylmethylamine in Methanol[a]

temp, 23 °C		temp, 120 °C	
time, h	ratio 7/8	time, h	ratio 7/1/(8+5)[b]
20	98.6/1.4 (±0.5)	1.0	64.0/ND/36.0
48	98.5/1.5	20	32.7/17.5/49.9[c]
144	95.7/4.3	48	24.1/25.0/50.9[c]

[a] $[7]_0 = [4]_0 = 0.289$ M. [b] SEC peaks for 8 and 5 are not separated. [c] Area % ratios from SEC. 7 and 8 have the same molar response factors, as do 1 and 5.

heating at 120 °C, the ratio of ester/amide increases. While it is clear that interconversion of amides 7 and 8 is faster than alcoholysis of the amides to form the esters, the concommitant ester formation makes analysis at higher conversions difficult. The corresponding reaction at room temperature proceeds much more slowly (Table III), with less than 5% of the original charge of 7 converted to 8 in one week, during which time no methyl ester is observed.

Kinetic Analysis: Rate and Equilibrium Constants. The equilibration experiments starting with ester 1 and amine 4 demonstrate that the equilibrium constant, K_e, is unity. This simplifies the kinetic analysis by requiring that the individual equilibrium constants for dissociation of esters 1 and 5 be identical, $K_e' = K_e''$. This requires

$$1 + 4 \rightleftharpoons 2 + 5$$

$$K_e = \frac{[2][5]}{[1][4]}$$

$$2 + 3 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} 1$$

$$K_e' = \frac{[1]}{[2][3]}$$

$$4 + 3 \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} 5$$

$$K_e'' = \frac{[5]}{[4][3]}$$

that the ratios of the rate constants be equal: $k_1/k_{-1} = k_2/k_{-2}$. It seems chemically reasonable that $k_1 = k_2$ and $k_{-1} = k_{-2}$, and this may be shown by a simple competitive alkylation experiment. Treatment of an equimolar methanol solution of amines 2 and 4 with methyl acrylate sufficient to consume only half of the total amine concentration gives a 1/1 mixture of 1 and 5, as well as unreacted amines. This is not due to equilibration, as reaction is complete in less than 30 min at room temperature, while complete equilibrium would take weeks. By use of this information, a steady-state assumption for the concentration of 3, and the initial condition $[1]_0 = [4]_0$, the rate expression for disappearance of 1 (eq 1) can be rewritten as eq 2. Integration gives eq 3.

$$\frac{-d[1]}{dt} = k_{-1}[1] - k_1[2][3] \quad (1)$$

$$\frac{-d[1]}{dt} = k_{-1}(2[1] - [1]_0) \quad (2)$$

$$\ln (2[1]_t - [1]_0) - \ln [1]_0 = 2k_{-1}t \quad (3)$$

A plot of the concentration term vs. time should then give a straight line of slope $= -2k_{-1}$, which then gives the reversion rate constant for esters 1 and 5. This plot is shown in Figure 1, and is indeed linear ($r = 0.998$), giving a reversion rate constant $k_{-1} = k_{-2} = 1.8 \times 10^{-6}$ s^{-1}.[6]

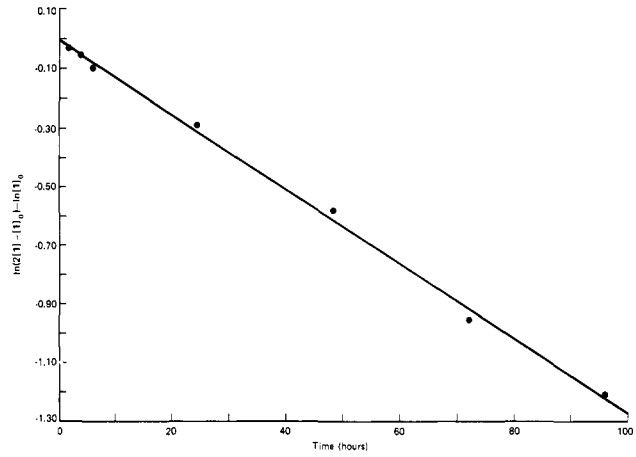


Figure 1. Kinetic plot of reaction of 1 with octadecylmethylamine at 23 °C.

A similar treatment of the data from the amides 7 and 8 should allow determination of the reversion rate constants for these compounds. In this case the equilibrium composition cannot be proven to be 1/1 due to competitive esterification of the amides, although the data strongly suggest it. A competitive alkylation experiment with acrylamide and amines 2 and 4 shows that the addition rates are identical, as with the corresponding esters. Equation 3 then applies, substituting [7] for [1], and a plot is linear ($r = 0.999$), yielding a reversion rate constant, $k_{-1} = 8.8 \times 10^{-8}$ s^{-1}.[6]

With the rate constants for reversion known, a simple measure of the forward rate constants gives us the equilibrium constants. The forward rate constant, k_1, for ester 1 was measured at room temperature in methanol by reacting equimolar 2 and 3, and analyzing for formation of 1. The kinetics of this type of reaction have been previously shown to be second order, and a plot is linear ($r = 0.98$), giving $k_1 = k_2 = 3.5 \times 10^{-2}$ L mol^{-1} s^{-1}.[6]

The rate constant for the addition to acrylamide may be extracted from the competitive alkylation experiment. For the reaction in eq 4, the integrated rate equation is given by eq 5.[7] Since the two amines have the same

$$aA + bB \rightarrow \text{products} \qquad a = b = 1,\ [A]_0 \neq [B]_0 \quad (4)$$

$$\ln \frac{[A][B]_0}{[A]_0[B]} = ([A]_0 - [B]_0)kt \quad (5)$$

$$\ln \frac{([2]_0 + [4]_0)([6]_0 - ([8] + [7]))}{[6]_0(([2]_0 + [4]_0) - ([8] + [7]))} = ([6]_0 - ([2]_0 + [4]_0))kt \quad (6)$$

addition rate, they may be combined as reactant B, with A being acrylamide. Making this substitution gives eq 6. A plot of eq 6 is linear ($r = 0.998$), giving a rate constant for addition of $k = 6.4 \times 10^{-4}$ L mol^{-1} s^{-1}.[6]

Incorporation of these rate constants in the expression $K_{eq} = k_f/k_r$ gives equilibrium constants of 2.0×10^4 L mol^{-1} and 7.3×10^3 L mol^{-1} (±15%) for the esters and amides, respectively. Since the equilibrium constant has a linear term divided by a squared term, the mole fraction of dissociated material is dependent on the concentration. Simple calculations (Table IV) reveal that even at relatively high concentrations, a percent or more of the material should be dissociated. These concentrations were in fact detectable by ^{1}H NMR, and are shown in Table IV

(6) Errors in rate constants are ±10%.

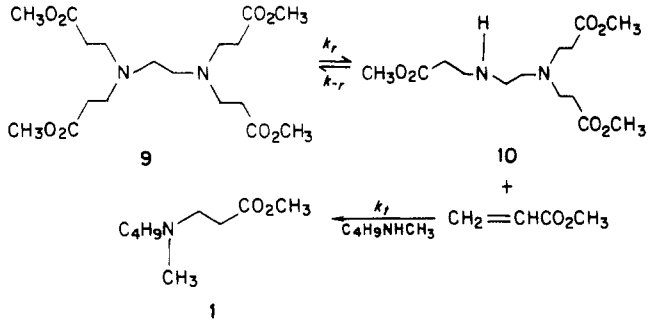
(7) Daniels, F.; Alberty, R. A. "Physical Chemistry"; Wiley: New York, 1966; p 330.

Table IV. Fraction of Material Dissociated at 23 °C in Methanol for 1 and 7

compd	concn., M	% dissociated from K_{eq}[a]	% dissociated from ^1H NMR[b,c]
1	0.94	0.73	1.2
1	0.16	1.8	2.0
1	0.022	4.6	3.9
7	1.02	1.2	1.5

[a] Error is ±15%. [b] Measured from the ratio of integrals of 3/1 or 6/7. Error is ±15%. [c] CD_3OD solvent.

Scheme II

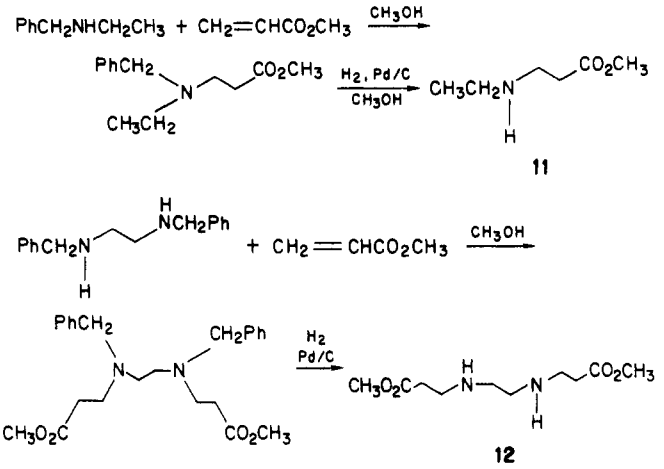


for several different concentrations of ester 1, and at one concentration of amide 7. As predicted, the fraction dissociated increases at lower concentrations, and the values agree reasonably well with those calculated from the equilibrium constants.

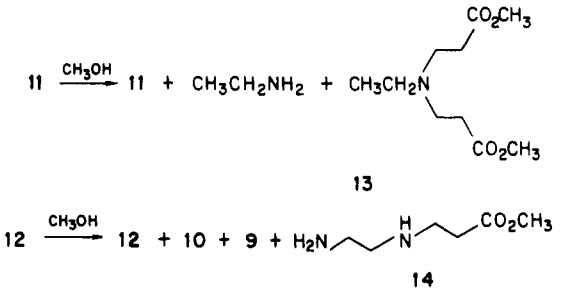
Eliminations from Other β-Amino Esters. In addition to the simple model systems, eliminations from several other β-amino esters were examined. An alternate approach to obtaining rate constants for these reactions is to trap the methyl acrylate with another nucleophile which reacts much faster than the amine formed by elimination. An example of this is shown in Scheme II. Compound 9, prepared by reaction of ethylenediamine and excess methyl acrylate, is allowed to equilibrate with methylbutylamine. In this case the rate of addition of the added amine is much faster than the addition of 10.[8] Under these conditions disappearance of 9 is a simple first-order reaction, at low conversion. A plot of ln $([9]_0/[9])$ vs. time is linear ($r = 0.999$) and gives a rate constants of reversion, $k_1 = 1.5 \times 10^{-6}$ s^{-1} at 23 °C. Even after correction for the statistical factor for the additional functional groups per molecule, this is only modestly slower than the rate of reversion of 3. This is in striking contrast to the addition rates, where 2 reacts with methyl acrylate ~300 times as fast as 10.[9]

The other two amino esters studied are secondary amines, formally derived from addition of primary amines to methyl acrylate. It is more difficult to determine rate constants in these cases, since both the starting material and reversion product may effectively compete with added nucleophiles for the methyl acrylate. The two compounds examined and their syntheses are shown in Scheme III. Attempts to react the primary amines directly with methyl acrylate invariably result in mixtures of mono- and dialkylated products which are very difficult to separate. Use of the benzyl protecting group avoids this problem, and debenzylation occurs cleanly in several hours at room temperature to give the desired products.[10,11] In the absence of added traps, a methanol solution of 11 gives a mixture containing ethylamine, the dialkylated material 13, and starting 11 (Scheme IV). Similarly, 12 reacts to give a mixture containing at least four of the possible alkylated ethylenediamines[12,13] as well as amides formed by reaction of primary amines with the methyl esters. In the presence of methylbutylamine as a trap, 11 and 12 given none of the higher alkylated materials. The decompositions under these conditions are first order early in the reaction, but as the concentrations of ethylamine and 14 increase, these effectively compete with the added trap for the methyl acrylate (Scheme V). From the initial slopes of first-order plots of the disappearance of 11 and 12, reversion rate constants may be estimated. For 11, $k_r \approx 7.5 \times 10^{-7}$ s^{-1} and for 12, $k_r \approx 1.2 \times 10^{-6}$ s^{-1}. After correction for the number of functional groups present in 12, these are identical within experimental error.

Scheme III



Scheme IV



Scheme V

$$11 + C_4H_9NHCH_3 \rightleftharpoons CH_3CH_2NH_2 + 1$$

$$12 + C_4H_9NHCH_3 \rightleftharpoons 14 + 1$$

Experimental Section

Proton NMR spectra were recorded on either a Varian EM 390 at 90 MHz, a Varian T60 at 60 MHz, or a Nicolet NT-300 at 300 MHz. Infrared spectra were recorded on a Perkin-Elmer 598 spectrophotometer. Melting points were determined on a Fish-

(8) Johnson, M. R., unpublished results.
(9) Johnson, M. R., unpublished results. This ratio was determined in methanol-d_4, and is therefore subject to different kinetic isotope effects on the two reactions. While a substantial isotope effect is expected, it should still be small compared to the reactivity differences.

(10) (a) Freifelder, M. "Practical Catalytic Hydrogenation"; Wiley-Interscience: New York, 1971, pp 413–428. (b) Mattocks, A. M.; Hartung, W. H. *J. Am. Chem. Soc.* **1946**, *68*, 2108.
(11) Haydock, D. B.; Mulholland, T. P. C. *J. Chem. Soc. C* **1971**, 2389.
(12) Authentic 14 was prepared according to Martell, A. E.; Chaberek, S. *J. Am. Chem. Soc.* **1950**, *72*, 5357. This material readily polymerizes by ester aminolysis: Wilson, L. R.; Tomalia, D. A., unpublished results.
(13) Authentic 10 was prepared from *N*-benzylethylenediamine. The geminally dialkylated ethylenediamine was not detected in the reaction mixture.

er-Johns hot stage apparatus. Elemental analysis was done by the Analytical Laboratories of the Dow Chemical Co.

Kinetics. Reactions at 120 °C were run in a 45-mL magnetically stirred stainless steel Parr reactor, and those at 23 °C were run in small unstirred glass vials. All reactions were analyzed by size-exclusion chromatography using two 30-cm 100-Å μ-Styragel columns with THF as eluent. Injection was done using a 10-μL constant-volume Rheodyne loop injector, with detection by a Perkin-Elmer LC-75 UV detector operating at 220 nm. Fast reactions were monitored by removing an aliquot of the reaction mixture, diluting in THF, and storing at −78 °C until analysis.

Reaction of Methylbutylamine with Methyl Acrylate. A solution of 5.00 g (57.5 mmol) of methylbutylamine in 20 mL of methanol was treated with 4.94 g (57.5 mmol) of methyl acrylate, and stirred overnight at room temperature. Solvent removal under reduced pressure yielded the pure amino ester **1**: ^{1}H NMR ($CDCl_3$) δ 0.85 (3 H, t), 1.30 (4 H, m), 2.20 (3 H, s), 2.25–2.80 (6 H, m), 3.65 (3 H, s). Anal. Calcd for $C_9H_{19}NO_2$: C, 62.4; H, 11.05; N, 8.08. Found: C, 62.1; H, 10.93; N, 8.28.

Reaction of Octadecylmethylamine with Methyl Acrylate. A solution of 1.50 g (5.30 mmol) of methyloctadecylamine in 12 mL of methanol was treated with 0.91 g (10.6 mmol) of methyl acrylate and stirred overnight at room temperature. Solvent and excess methyl acrylate were removed under reduced pressure to yield the pure amino ester **5** as a clear liquid: ^{1}H NMR ($CDCl_3$) δ 0.85 (3 H, br t), 1.35 (32 H, br s), 2.20 (3 H, s), 2.25–2.80 (6 H, m), 3.65 (3 H, s). Anal. Calcd for $C_{23}H_{47}NO_2$: C, 74.4; H, 12.82; N, 3.79. Found: C, 74.6; H, 12.80; N, 3.82.

Reaction of Octadecylmethylamine with Acrylamide. A solution of 2.0 g (7.07 mmol) of octadecylmethylamine in 10 mL of methanol was treated with 0.50 g (7.04 mmol) of acrylamide at room temperature. After 1 h a white precipitate had formed. The mixture was stirred at room temperature for 3 days, and the precipitate was collected by filtration and dried under vacuum to give **8**: mp 77.5–78 °C; ^{1}H NMR ($CDCl_3$) δ 0.90 (3 H, m), 1.1–1.5 (32 H, m), 2.15 (3 H, s), 2.20–2.80 (6 H, s), 5.70 (1 H, br s), 8.10 (1 H, br s). Anal. Calcd for $C_{22}H_{46}N_2O$: C, 74.5; H, 13.07; N, 7.90. Found: C, 74.4; H, 12.96; N, 7.95.

Reaction of Methylbutylamine with Acrylamide. A solution of 5.0 g (70.4 mmol) of acrylamide in 15 mL of methanol was treated with 6.74 g (77.5 mmol) of methylbutylamine and stirred at room temperature for 24 h. Solvent removal under reduced pressure yielded the aminoamide **7** as a clear liquid: ^{1}H NMR ($CDCl_3$) δ 0.90 (3 H, br t), 1.10–1.60 (4 H, m), 2.20 (3 H, s), 2.20–2.70 (6 H, m), 6.20 (1 H, br s), 7.90 (1 H, br s). Anal. Calcd for $C_8H_{18}N_2O$: C, 60.7; H, 11.50; N, 17.70. Found: C, 60.1; H, 11.50; N, 17.50.

Reaction of Ethylenediamine with Methyl Acrylate. A solution of 10.0 g (167 mmol) of ethylenediamine in 100 mL of methanol was chilled in an ice bath and treated with 60.2 g (700 mmol) of methyl acrylate, added in three portions over a period of 1 h. The solution was stirred at room temperature for 3 days, and then the solvent was removed under reduced pressure to yield amino ester **9** as a clear oil. SEC analysis indicated a small quantity (<2%) of the trialkylated material **10** as the only significant impurity: ^{1}H NMR ($CDCl_3$) δ 2.30–2.85 (16 H, m), 2.45 (4 H, s), 2.60 (12 H, s). Anal. Calcd for $C_{18}H_{32}N_2O_8$: C, 53.4; H, 7.98; N, 6.93. Found: C, 53.5; H, 7.93; N, 6.97.

Reaction of *N,N'*-Dibenzylethylenediamine with Methyl Acrylate. A solution of 3.0 g (12.5 mmol) of *N,N'*-dibenzylethylenediamine in 10 mL of methanol was treated with 2.26 g (26.3 mmol) of methyl acrylate, and stirred at room temperature for 3 days. Solvent was removed under reduced pressure to give the dialkylated material as a clear oil: ^{1}H NMR ($CDCl_3$) δ 2.25–2.90 (8 H, m), 2.60 (4 H, s), 3.55 (4 H, s), 3.60 (6 H, s), 7.25 (5 H, br s). Anal. Calcd for $C_{24}H_{32}N_2O_4$: C, 69.9; H, 7.82; N, 6.79. Found: C, 69.9; H, 7.78; N, 6.85. This material was debenzylated directly with no further purification.

Preparation of 12.[11] A slurry of 0.5 g of 5% Pd/C in 35 mL of methanol was treated with 1.7 g (4.1 mmol) of the dialkylated dibenzylethylenediamine from the previous experiment in 5 mL of methanol. The slurry was magnetically stirred under balloon pressure of hydrogen with periodic monitoring by SEC. After 13 h, the mixture was filtered and solvent removed under reduced pressure to yield **12** as a clear oil. **12** crystallized upon storage in a freezer, but melted upon warming to room temperature: ^{1}H NMR ($CDCl_3$) δ 1.60 (2 H, br s), 2.25–2.90 (8 H, m), 2.65 (4 H, s), 3.60 (6 H, s).

Reaction of Benzylethylamine with Methyl Acrylate. A solution of 3.0 g (22.2 mmol) of benzylethylamine in 10 mL of methanol was treated with 2.1 g (24.4 mmol) of methyl acrylate and stirred at room temperature overnight. Solvent was removed under reduced pressure to yield a clear oil: ^{1}H NMR ($CDCl_3$) δ 1.00 (3 H, t), 2.30–2.90 (6 H, m), 3.50 (2 H, s), 3.60 (3 H, s), 7.20 (5 H, br s). Anal. Calcd for $C_{13}H_{19}NO_2$: C, 70.6; H, 8.65; N, 6.33. Found: C, 70.6; H, 8.48; N, 6.32.

Preparation of Methyl 3-(Ethylamino)propionate. A slurry of 0.25 g of 5% Pd/C in 20 mL methanol was treated with a solution of 1.0 g (4.52 mmol) of the amine from the previous experiment in 1.0 mL of methanol. The mixture was stirred under balloon pressure of hydrogen at room temperature with SEC monitoring. After 9 h the mixture was filtered, and solvent was removed under reduced pressure to yield **11** as a clear oil: ^{1}H NMR (CD_3CN) δ 1.0 (3 H, t), 1.25 (1 H, br s), 2.20–2.90 (6 H, m), 3.60 (3 H, s). SEC analysis indicated >98% purity with the only detected contaminant the benzylated precursor.

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